Remarks

The Office Action mailed September 19, 2001, has been received and reviewed. Claims 1 through 12 and 14 through 21 are currently pending in the application, and each of claims 1 through 12 and 14 through 21 stand rejected. Applicants have added new claims 21 through 28. Applicants respectfully request reconsideration of the application in light of the amendments and remarks included herein.

35 U.S.C. § 102(b) Rejections

Claims 1 through 12, 14, 15, and 17 through 21 stand rejected as being anticipated by Tkachuk et al. (hereinafter "Tkachuk"). Applicants respectfully traverse the rejection.

Tkachuk discloses a first probe ("PEM12") to the normal *bcr* chromosome that overlaps the breakpoint cluster region (Tkachuk, p. 560, FIG. 1 – top drawing, lines 17-19). As shown in FIG. 1, the PEM12 probe (depicted by the open horizontal bar) lies ***within*** the breakpoint region (depicted as a dashed line) of *bcl*. A second probe (*i.e.*, c-H-abl) to the normal *abl* chromosome is separated from the breakpoint cluster region of the second gene by a distance of between 25-200 base pairs (*Id.*, p. 560, FIG. 1 – second drawing, lines 23-24).

Tckachuk further discloses a method of using the specific probes that includes utilizing two different probes directed to specific portions near the known breakpoint region on **two different chromosomes**. The two probes may be labeled with two differently colored signals such that in a normal chromosome, four distinct (two of each color for each probe) and separate signals will appear. (Tkachuk, page 560, last full paragraph in left col.). In leukemia, the *bcr* chromosome and *abl* chromosome break and one the fragments of each chromosome join to form a fused gene. (Tkachuk, FIG. 1- third drawing). After fusion, the labeled PEM12 probe and labeled c-H-abl probe will be so close that the signals co-localize. (Tkachuk, page 560, second column). Thus, the Tkachuk method detects an aberrant chromosome (the fusion of the two chromosomes) by detecting the co-localization of two probes.

The Tkachuk probes are in stark contrast to the presently claimed invention wherein probes flank (*i.e.*, are located on the side of) the breakpoint cluster region (*e.g.*, equidistant to the breakpoint region) **on a single chromosome** and do not lie within or span or overlap the breakpoint cluster region on a chromosome. In the present invention, the pair of probes flank opposing sides of a breakpoint region on a single chromosome and, thus, appears as a co-

localized signal in a **normal** chromosome. However, if an aberration occurs (*i.e.*, a break in the breakpoint region) the two probes will be separated and thus appear as two separate signals. Tkachuk clearly does not disclose the pair of nucleic acid probes or the method of the present invention.

Applicants respectfully submit that one of skill in the art would clearly understand that the claims are clearly directed to a **pair** of nucleic acid probes that flank either side of a potential breakpoint on a **single** chromosome. However, in an effort to expedite examination, applicants have amended independent claims 1, 2, 11 and 12 to recite a pair of nucleic acid probes "flanking a potential breakpoint in a single chromosome". Support for the amendment may be found in the Specification, for example, page 6, line 25 through page 7, line 5. Applicants respectfully submit that Tkachuk fails to disclose this element of the claims. At best, Tkachuk only discloses probes on either side of a **fusion** region of an aberrant chromosome, but does not disclose a pair of nucleic acid probes flanking a potential **breakpoint** region on a single chromosome. (Tkachuk, FIG. 1, third drawing from top of page).

Additionally, independent claim 1 recites that each probe is "labeled with at least one different reporter molecule such that a split signal arises after a break within said potential breakpoint". Applicants respectfully submit that Tkachuk fails to disclose this element of the claims. As stated, Tkachuk detects co-localization of two signals.

As Tkachuk fails to disclose every element of the present invention, claims 1 through 12, 14, 15 and 17 through 21 are not anticipated by Tkachuk. Reconsideration and withdrawal of the rejection is requested.

Claim 16 stands rejected under 35 U.S.C. §102(b), as assertedly being anticipated by Rowley et al. (hereinafter "Rowley"). The kits disclosed by Rowley, however, do not provide a pair of probes as described in claim 1. Rowley discloses four nucleic acid probes; MLL 0.7B (SEQ ID NO: 1) is .7 kb, MLL 0.3BE (SEQ ID NO: 2) is .3 kb, MLL 1.5SEB (SEQ ID NO: 3) is 1.5 kb and 14-7 (SEQ ID NO: 5) is 1.3 bp. In contrast with claim 1, MLL 0.7B (SEQ ID NO: 1) and MLL 0.3BE (SEQ ID NO: 2) are **smaller than 1 kb**. In further contrast with claim 1, neither 14-7 (SEQ ID NO: 5) nor MLL 0.7B (SEQ ID NO: 1) flank the breakpoint region. (*See*, FIG. 2). Accordingly, neither MLL 0.7B (SEQ ID NO: 1), MLL 0.3BE (SEQ ID NO: 2), nor 14-7 (SEQ ID NO: 5) anticipate claim 16.

Thus, only MLL 1.5SEB (SEQ ID NO: 3) remains from the Rowley disclosure.

However, MLL 1.5SEB (SEQ ID NO: 3) is a single nucleic acid probe located on one side of a breakpoint, not a pair of nucleic acid probes having comparable size, flanking a potential breakpoint on a chromosome being labeled with at least one different reporter molecule such that a split signal arises after a break in said breakpoint region as recited in claim 1 from which claim 16 depends.

As Rowley fails to disclose every element of claim 16, Rowley cannot anticipate claim 16. Reconsideration and withdrawal of the rejection is requested.

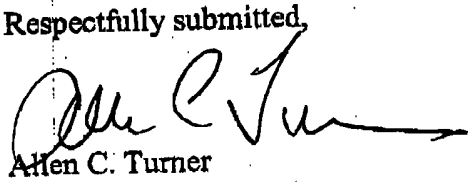
New claims

Applicants have added new claims 21 through 28. Dependent claims 22 through 28 are substantially similar to pending claims 3 and 5 through 10. Support for the claims may also be found in the as-filed Specification and claims at least, for example, page 6, lines 4-20; page 6, lines 25-27; page 7, lines 1-2; page 8, lines 8-13; page 13, lines 26-27; page 14, lines 1-16. Applicants respectfully submit that new claims 21 through 28 avoid the references cited herein at least for substantially the same reasons as discussed herein.

Conclusion

Claims 1 through 12 and 14 through 28 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, she is respectfully invited to contact Applicant's undersigned attorney.

Respectfully submitted,



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Date: March 18, 2002

APPENDIX A

VERSION WITH MARKINGS SHOWING CHANGES MADE

1. (Amended four times) A pair of nucleic acid probes having comparable size, said size being selected from the group consisting of from 1 to 100 kb, from 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb, and 80 to 100 kb, and flanking a potential breakpoint in a single chromosome, each of said pair of probes being [labelled] labeled with at least one different reporter molecule such that a split signal arises after a break within said potential breakpoint.

2. (Amended four times) A pair of nucleic acid probes of comparable size, said size being selected from the group consisting of from 1 to 100 kb, from 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb, and 80 to 100 kb, and flanking a potential breakpoint in a single chromosome, which pair of nucleic acid probes hybridize to a nucleic acid molecule at a genomic distance of from about 50 kb to no more than 100 kb.

4. (Amended four times) The pair of nucleic acid probes of claim 2, each of said pair of nucleic acid probes being [labelled] labeled directly or indirectly with at least one reporter molecule.

6. (Amended four times) The pair of nucleic acid probes of claim 5 wherein the pair of nucleic acid probes hybridize to a single corresponding nucleic acid molecule.

11. (Amended four times) A method of detecting a nucleic acid molecule having a chromosomal aberration, said method comprising:

providing a pair of nucleic acid probes to analyze a sample believed to contain said nucleic acid, said pair of nucleic acid probes having comparable size, said size being selected from the group consisting of 1 to 100 kb, 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb and 80 to 100 kb, and said pair of nucleic acid probes flanking a potential breakpoint in a single chromosome,

each of said pair of nucleic acid probes being labeled with at least one different reporter molecule;

hybridizing said pair of nucleic acid probes to said nucleic acid; and

detecting the presence of said at least one different reporter molecule.

12. (Amended) A method of detecting cells suspected of having a chromosomal aberration, said method comprising:

providing a pair of nucleic acid probes to analyze nucleic acid of said cells, said pair of nucleic acid probes having comparable size, said size being selected from the group consisting of 1 to 100 kb, 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb and 80 to 100 kb, and said pair of nucleic acid probes flanking a potential breakpoint in a single chromosome, each of said pair of nucleic acid probes being labeled with at least one different reporter molecule;

hybridizing said pair of nucleic acid probes to the nucleic acid of at least one of said cells; and

detecting the presence of said at least one different reporter molecule.

17. (Amended three times) The pair of nucleic acid probes of claim 1, wherein the pair of nucleic acid probes hybridize to a single corresponding nucleic acid molecule.